Case Report

Three cases of heparin-induced thrombocytopenia associated with polytrauma

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Case: We present three cases in which patients that had suffered polytrauma developed heparin-induced thrombocytopenia after the start of heparin treatment for thrombosis. All three patients had high injury severity scores and required major surgery. They all started receiving unfractionated heparin for deep venous thrombosis with or without an asymptomatic pulmonary embolism. The patients were clinically diagnosed with heparin-induced thrombocytopenia after their platelet counts fell or exhibited a delayed recovery.

Outcome: Heparin-induced thrombocytopenia and the associated thromboses were successfully treated by discontinuing all forms of heparin treatment and administering argatroban followed by warfarin.

Conclusion: Early recognition and clinical diagnosis of heparin-induced thrombocytopenia is necessary for clinicians in cases in which severely injured trauma patients show reductions or delayed recovery in their platelet counts in combination with thrombosis after starting heparin treatment.

Key words: Argatroban, deep venous thrombosis, heparin-induced thrombocytopenia, polytrauma, warfarin

INTRODUCTION

IT HAS BEEN reported that more than half of major trauma patients develop postoperative thromboemboli.[1] However, heparin-induced thrombocytopenia (HIT) only occurs in 0.5% of critically ill patients receiving unfractionated heparin (UFH) or low-molecular-weight heparin for thromboprophylaxis.[2] We present three instructive cases of HIT associated with polytrauma.

CASES

Case 1

A 62-YEAR-OLD MALE WAS transferred from another hospital after being run over by a car. His vital signs on arrival were: Glasgow Coma Scale, 15; respiratory rate, 26 breaths/min; pulse rate (PR), 136 b.pm.; and blood pressure (BP), 88/45 mmHg. He had multiple bilateral rib fractures, a clinically unstable pelvic fracture, and multiple transverse process fractures of the lumbar vertebrae, which caused him to go into hemorrhagic shock; however, this was successfully controlled using transcatheter arterial embolization and external fixation of the pelvis. On day 12, a catheter-related deep venous thrombosis (DVT) extending from the left jugular vein to the superior vena cava was detected. After starting UFH treatment, the patient's platelet count subsequently dropped from 19.3 to $10.1 \times 10^4/\mu L$ over 3 days (Fig. 1A). As we considered HIT to be a possibility, we discontinued the heparin infusion and treated the patient with argatroban. Heparin-induced thrombocytopenia was definitely diagnosed several days later using antigen (optical density of the anti-PF4/heparin IgG antibody (Ab), 1.655; cut-off point, 0.400) and functional assays. Although an asymptomatic pulmonary embolism had been detected on day 23, the HIT with thrombosis (HITT) was successfully treated with argatroban, and the patient was switched to warfarin thereafter. The patient was transferred to another hospital on the 31st hospital day.

Case 2

A 61-year-old female was transferred from another hospital after a car crash. She presented with cardiac tamponade and

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Received 17 Dec, 2014; accepted 20 Mar, 2015; online publication 28 May, 2015

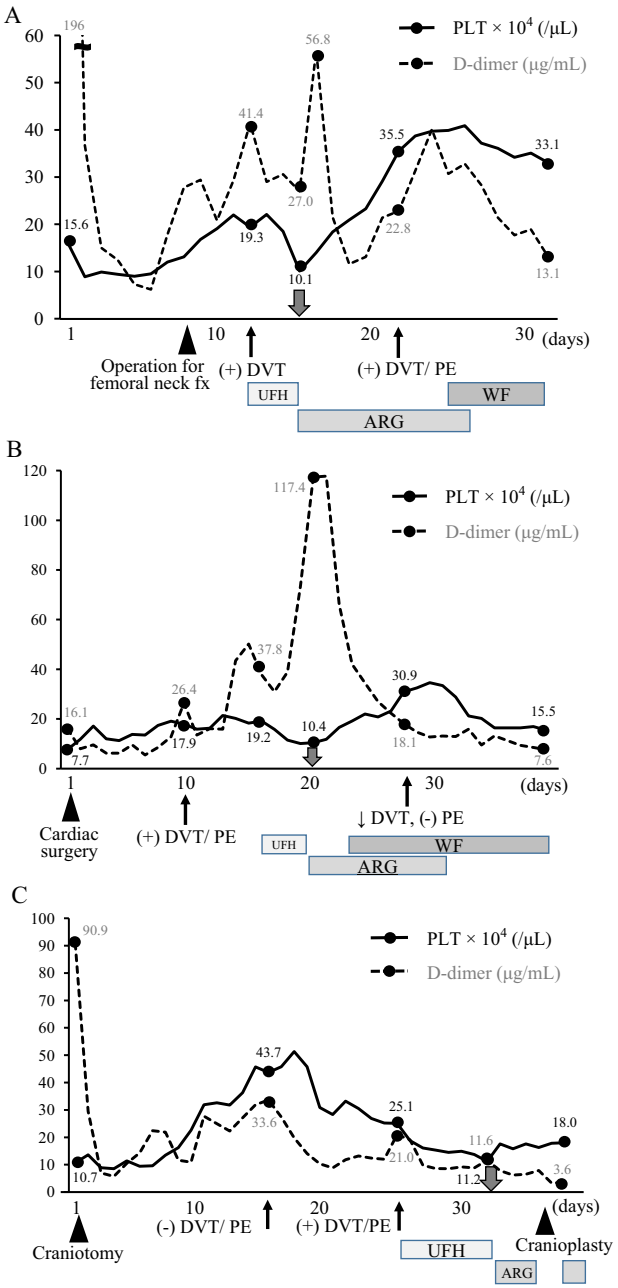

Fig. 1. Clinical courses of three cases of heparin-induced thrombocytopenia (HIT) including the patients' daily platelet counts (PLT) and D-dimer levels. A: Case 1. B: Case 2. C: Case 3. The downward-pointing arrows indicate the day on which HIT was clinically diagnosed. ARG, argatroban; DVT, deep venous thrombosis; fx, fracture; PE, pulmonary embolism; UFH, unfractionated heparin; WF, warfarin.

the following vital signs: PR, 160 b.p.m.; BP, 60/40 mmHg (already intubated). Her ruptured left atrium was successfully repaired whilst she was on a cardiopulmonary bypass. On day 10, a DVT extending from the left external iliac vein to the femoral vein and a pulmonary embolism were detected. Due to the coexisting traumatic dissection of the descending aorta, UFH treatment for the DVT was started 6 days after the condition was first detected. Despite anticoagulation therapy, the patient's elevated D-dimer levels and declining platelet count (from 19.2 to $10.4 \times 10^4/\mu L$) resulted in a clinical diagnosis of HIT and the cessation of UFH treatment (Fig. 1B). Argatroban was initiated followed by warfarin for HITT. Several days later, the patient was definitely diagnosed with HIT using antigen (optical density of the anti-PF4/heparin IgG Ab, 2.602) and functional assays. Although a minor asymptomatic intracranial hemorrhage was detected on a follow-up computed tomography scan, the patient's HITT was successfully treated. The patient was transferred to another hospital on the 58th hospital day.

Case 3

A 77-year-old female was moved from another hospital after a fall from a height of 2 m. Her vital signs on arrival were: Glasgow Coma Scale, 9 (E1V3M5); respiratory rate, 26 breaths/min; PR, 92 b.p.m.; and BP, 110/68 mmHg. A craniotomy was carried out immediately to remove a subdural hematoma. On day 15, a pulmonary embolism and a DVT extending from the right external iliac vein to the lower extremities were detected so UFH treatment was started. The patient's platelet count subsequently dropped from 25.1 to $11.2 \times 10^4/\mu L$ over the course of 1 week, which led us to strongly suspect HIT (Fig. 1C). The patient's HITT was treated with argatroban followed by warfarin. The patient was definitely diagnosed with HIT using antigen (optical density of the anti-PF4/heparin IgG Ab, 1.714) and functional assays. She was transferred to another hospital on the 68th hospital day.

Table 1 shows a summary of the three cases.

DISCUSSION

HEPARIN-INDUCED THROMBOCYTOPENIA INVOLVES the immune-mediated aggregation of platelets. This can lead to thrombocytopenia, which in turn can bring about arterial and venous thrombotic complications including pulmonary embolisms, ischemic limb necrosis, and myocardial and cerebral infarctions.[2] The incidence of HIT is approximately ≤1% among patients receiving heparin.[3] Although low-molecular-weight heparin is

Table 1. Summary of three cases of heparin-induced thrombocytopenia (HIT) complicated with polytrauma

Case	Age, years	Sex	Mechanism of injury	ISS	Injury	Start day of heparin treatment for DVT	Day of clinical diagnosis for HIT	4Ts score on the day of clinical diagnosis	Complication of anticoagulant
1	62	M	MVA	41	Multiple rib fractures, multiple transverse process fractures of lumbar pelvic fracture, femoral neck fracture	12	15	5	None
2	61	F	MVA	50	Cardiac rupture, traumatic SAH, traumatic dissection of the descending aorta, multiple rib fractures, pelvic fracture	16	20	6	Asymptomatic exacerbation of traumatic SAH
3	77	F	Fall	45	SDH, temporal bone fracture, multiple rib fractures, liver injury	26	33	5	None

DVT, deep venous thrombosis; F, female; ISS, injury severity score; M, male; MVA, motor vehicle accident; SAH, subarachnoid hemorrhage; SDH, subdural hematoma.

associated with a lower risk of HIT than UFH, both treatments can cause the condition, as can heparin flushes and saline solutions containing heparin, which are used for continuous blood pressure monitoring.[3,4] Among trauma patients, major surgery causes HIT more frequently than minor surgery.[5] All three of the patients presented in this study were severely injured and underwent major surgery.

The 4Ts scoring system, which assesses thrombocytopenia, the timing of platelet count reductions or thrombosis, thrombosis or other clinical sequelae, and other causes of thrombocytopenia, is widely used for screening.[6] Although HIT can be ruled out when a low 4T score is obtained, definitive diagnoses should be based on a combination of compatible clinical findings and serological testing, including antigen and functional assays, to prevent overdiagnosis.[7–9] It is recommended to discontinue UFH treatment or switch to argatroban as soon as possible when a moderate to high 4Ts score is obtained.

Various problems can arise during the treatment of polytrauma and HIT. First, it is sometimes difficult to exclude other causes of thrombocytopenia in critically ill patients. Second, the incidence of DVT is high after polytrauma and so UFH treatment, which is safe for use in severely injured trauma patients with intracranial hemorrhages or coagulopathy (as was seen in the present three cases), is often started. This can make it difficult to determine whether a thrombosis was caused by DVT or HIT. However, in case 2, HIT was suspected at an early stage due to the delayed recovery of the patient's platelet count.

If HIT is strongly suspected, all forms of heparin should be stopped, and argatroban followed by warfarin should be given in cases involving thrombosis.

CONCLUSION

CLINICIANS SHOULD TAKE HIT into consideration as early as possible in cases in which severely injured trauma patients show reductions in their platelet counts (or the delayed recovery of their platelet counts) in combination with thrombosis after receiving heparin treatment to prevent developing HITT.

CONFLICT OF INTEREST

NONE.

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